WEST

The Contents of Case 09658699

Qnum	Query	DB Name	Thesaurus	Operator	Plural
Q1	(oppmann)[IN]	USPT,PGPB,JPAB,EPAB,DWPI	None	OR	YES
Q2	(oppmann)[IN] or (de waal malefyt)[in] or (rennick)[in] or (kastelein) [in] or (wickowski)[in] or (lira)[in] or (narula)[in]	USPT,PGPB,JPAB,EPAB,DWPI	None	OR	YES
Q3	Q2 and ((IL adj 12 adj P40) or (IL adj B30))	USPT,PGPB,JPAB,EPAB,DWPI	None	OR	YES
Q4	((IL adj 12 adj P40) or (IL adj B30))	USPT,PGPB,JPAB,EPAB,DWPI	None	OR	YES
Q5	((IL adj 12 adj P40) and(IL adj B30))	USPT,PGPB,JPAB,EPAB,DWPI	None	OR	YES
Q6	((IL adj 12 adj P40) and (IL adj B30))	USPT,PGPB,JPAB,EPAB,DWPI	None	OR	YES
Q7	(IL adj 12 adj P40) near antibod$4	USPT,PGPB,JPAB,EPAB,DWPI	None	OR	YES
Q8	il adj b30	USPT,PGPB,JPAB,EPAB,DWPI	None	OR	YES
Q9	Q8 near antibod$4	USPT,PGPB,JPAB,EPAB,DWPI	None	OR	YES

Run Case | Update Case | Cancel

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WEST Search History

DATE: Monday, May 13, 2002

Set Name side by side	Query	Hit Count	Set Name result set
	DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR		
L33	L32 near antibod$4	1	L33
L32	il adj b30	6	L32
L31	(IL adj 12 adj P40) near antibod$4	1	L31
L30	((IL adj 12 adj P40) and (IL adj B30))	1	L30
L29	((IL adj 12 adj P40) and(IL adj B30))	1	L29
L28	((IL adj 12 adj P40) or (IL adj B30))	64	L28
L27	L26 and ((IL adj 12 adj P40) or (IL adj B30))	4	L27
L26	(oppmann)[IN] or (de waal malefyt)[in] or (rennick)[in] or (kastelein)[in] or (wickowski)[in] or (lira)[in] or (narula)[in]	52987	L26
L25	(oppmann)[IN]	20	L25
~~L24~~	~~laminin same ((alpha adj 2) same (beta adj 1) same (gamma adj 3))~~	1	L24
L23	laminin adj 12	2	L23
L22	L21 and laminin	29	L22
L21	(burgeson)[IN] OR (champliaud)[IN] or (olsen) [inv] or (koch) [in] or (brunken) [in]	14084	L21
L20	(burgeson)[IN] OR (champliaud)[IN]	68	L20
L19	RO adj ssa	8	L19
	DB=USPT; PLUR=YES; OP=OR		
L18	4784942.pn.	1	L18
L17	4751181.pn.	1	L17
	DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR		
L16	(52KD or (52 adj kd) or (52 adj (52 adj kd))) near (RO$4)	3	L16
L15	(52KD or (52 adj kd) or (52 adj (52 adj kd)))	289	L15
L14	6111088	2	L14
L13	L10 and (52KD or (52 adj kd) or (52 adj (52 adj kd)))	17	L13
L12	L11 and (52KD or (52 adj kd) or (52 adj (52 adj kd)))	0	L12
L11	L10 and SLE	27	L11
L10	(Frank)[IN] OR (itoh)[IN]	80879	L10
L9	L8 and immunogen$4	2	L9
L8	L7 near (mutat$4 or alter$ or recomb$4 or modif$4)	29	L8
L7	streptokinase	3185	L7
L6	((less or decreas$4 or reduc$4) adj immunogen$8) same(class adj II)	9	L6

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     (FILE 'HOME' ENTERED AT 17:25:42 ON 13 M[illegible]002)

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 17:26:00 ON 13 MAY 2002
L1           46 S (ANTIBOD? OR FAB) (10N) ((IL-12 (1N) P40) OR (IL (1N) B30))
L2           46 S (ANTIBOD? OR FAB) (10N) ((IL-12 (1N) P40))
L3            1 S (ANTIBOD? OR FAB) (10N) ((IL (1N) B30))
L4            0 S L3 NOT L2
L5           15 DUP REM L2 (31 DUPLICATES REMOVED)
L6           14 S L5 NOT L3
L7         1800 S OPPMANN B?/AU OR DE WAAL MALEFYT R?/AU OR RENNICK D?/AU OR KA
L8          111 S L7 AND ((IL (1N) 12) OR (IB (1N) 30))
L9            9 S L7 AND ((IL (1N) 12 (1N) P40) OR (IB (1N) 30))
L10           4 DUP REM L9 (5 DUPLICATES REMOVED)
L11          11 S L7 AND ((IL (1N) 12 (1N) P40) OR (IL (1N) B30))
L12           6 DUP REM L11 (5 DUPLICATES REMOVED)

=> end
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y
COST IN U.S. DOLLARS                                 SINCE FILE      TOTAL
                                                          ENTRY    SESSION
FULL ESTIMATED COST                                      113.12     113.33

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)           SINCE FILE      TOTAL
                                                          ENTRY    SESSION
CA SUBSCRIBER PRICE                                       -4.34      -4.34

STN INTERNATIONAL LOGOFF AT 17:53:30 ON 13 MAY 2002
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WO 2001 85790

L8 ANSWER 4 OF 29 MEDLINE DUPLICATE 3

ACCESSION NUMBER: 2002286910 MEDLINE
DOCUMENT NUMBER: 22018121 PubMed ID: 12023338
TITLE: **IL-23** and IL-12 have overlapping, but distinct, effects on murine dendritic cells.

AUTHOR: Belladonna Maria Laura; Renauld Jean-Christophe; Bianchi Roberta; Vacca Carmine; Fallarino Francesca; Orabona Ciriana; Fioretti Maria Cristina; Grohmann Ursula; Puccetti Paolo
CORPORATE SOURCE: Department of Experimental Medicine, University of Perugia, Perugia, Italy.

SOURCE: JOURNAL OF IMMUNOLOGY, (2002 Jun 1) 168 (11) 5448-54.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200206
ENTRY DATE: Entered STN: 20020528
Last Updated on STN: 20020613
Entered Medline: 20020612

AB **IL-23** is a recently discovered heterodimeric cytokine that shares biological properties with proinflammatory cytokines. The biologically active heterodimer consists of p19 and the p40 subunit of IL-12. **IL-23** has been shown to possess biological activities on T cells that are similar as well distinct from those of IL-12. We have constructed single-chain **IL-23** and IL-12 fusion proteins (**IL-23**-Ig and IL-12-Ig) and have compared the two recombinant proteins for effects on murine dendritic cells (DC). Here we show that the **IL-23**-Ig can bind a significant proportion of splenic DC of both the CD8alpha(-) and CD8alpha(+) subtypes. Furthermore, IL-23and IL-12-Ig exert biological activities on DC that are only in part overlapping. While both proteins induce IL-12 production from DC, only **IL-23**-Ig can act directly on CD8alpha(+) DC to promote immunogenic presentation of an otherwise tolerogenic tumor peptide. In addition, the in vitro effects of **IL-23**-Ig did not appear to require IL-12Rbeta2 or to be mediated by the production of IL-12. These data may establish **IL -23** as a novel cytokine with major effects on APC.

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

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 NEWS  1         Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Jan 25  BLAST(R) searching in REGISTRY available in STN on the Web
 NEWS  3  Jan 29  FSTA has been reloaded and moves to weekly updates
 NEWS  4  Feb 01  DKILIT now produced by FIZ Karlsruhe and has a new update
                  frequency
 NEWS  5  Feb 19  Access via Tymnet and SprintNet Eliminated Effective 3/31/02
 NEWS  6  Mar 08  Gene Names now available in BIOSIS
 NEWS  7  Mar 22  TOXLIT no longer available
 NEWS  8  Mar 22  TRCTHERMO no longer available
 NEWS  9  Mar 28  US Provisional Priorities searched with P in CA/CAplus
                  and USPATFULL
 NEWS 10  Mar 28  LIPINSKI/CALC added for property searching in REGISTRY
 NEWS 11  Apr 02  PAPERCHEM no longer available on STN.  Use PAPERCHEM2 instead.
 NEWS 12  Apr 08  "Ask CAS" for self-help around the clock
 NEWS 13  Apr 09  BEILSTEIN: Reload and Implementation of a New Subject Area
 NEWS 14  Apr 09  ZDB will be removed from STN
 NEWS 15  Apr 19  US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
 NEWS 16  Apr 22  Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
 NEWS 17  Apr 22  BIOSIS Gene Names now available in TOXCENTER
 NEWS 18  Apr 22  Federal Research in Progress (FEDRIP) now available

 NEWS EXPRESS  February 1 CURRENT WINDOWS VERSION IS V6.0d,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
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FILE 'HOME' ENTERED AT 17:25:42 ON 13 MAY 2002

=> e medline caplus embase biosis
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
The EXPAND command is used to look at the index in a file
which has an index.  This file does not have an index.

=> file medline caplus embase biosis
COST IN U.S. DOLLARS                             SINCE FILE     TOTAL
                                                      ENTRY   SESSION
FULL ESTIMATED COST                                    0.21      0.21

FILE 'MEDLINE' ENTERED AT 17:26:00 ON 13 MAY 2002

FILE 'CAPLUS' ENTERED AT 17:26:00 ON 13 MAY 2002
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=> s (antibod? or Fab) (10N) ((IL-12 (1N) p40) or (IL (1N) B30))
L1          46 (ANTIBOD? OR FAB) (10N) ((IL-12 (1N) P40) OR (IL (1N) B30))

=> s (antibod? or Fab) (10N) ((IL-12 (1N) p40) and (IL (1N) B30))
PROXIMITY OPERATION NOT ALLOWED
PROXIMITY OPERATION NOT ALLOWED
PROXIMITY OPERATION NOT ALLOWED
PROXIMITY OPERATION NOT ALLOWED
Certain operators may not be nested in combination with other
operators.  A nested operator is valid only when it occurs at the same
level or above the operator outside the nested phrase as determined by
the following precedence list:

                    1.    Numeric
                    2.    (W), (NOTW), (A), (NOTA)
                    3.    (S), (NOTS)
                    4.    (P), (NOTP)
                    5.    (L), (NOTL)
                    6.    AND, NOT
                    7.    OR

For example, '(MONOCLONAL(W)ANTIBOD?)(L)ANTIGEN?' is valid since (W)
is above (L) on the precedence list.  However,
'((THIN(W)LAYER)(L)PHOSPHOLIPID#)(A)LACTONE#' is not valid since (L)
is below (A) on the precedence list.  The only exception is the 'OR'
operator.  This operator may be used in combination with any other
operator.  For example, '(ATOMIC OR NUCLEAR)(W)REACTOR' is valid.

=> s (antibod? or Fab) (10N) ((IL-12 (1N) p40) (P) (IL (1N) B30))
```

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PROXIMITY OPERATION NOT ALLOWED
PROXIMITY OPERATION NOT ALLOWED
PROXIMITY OPERATION NOT ALLOWED
PROXIMITY OPERATION NOT ALLOWED
Certain operators may not be nested in combination with other
operators.  A nested operator is valid only when it occurs at the same
level or above the operator outside the nested phrase as determined by
the following precedence list:

                    1.    Numeric
                    2.    (W), (NOTW), (A), (NOTA)
                    3.    (S), (NOTS)
                    4.    (P), (NOTP)
                    5.    (L), (NOTL)
                    6.    AND, NOT
                    7.    OR

For example, '(MONOCLONAL(W)ANTIBOD?)(L)ANTIGEN?' is valid since (W)
is above (L) on the precedence list.  However,
'((THIN(W)LAYER)(L)PHOSPHOLIPID#)(A)LACTONE#' is not valid since (L)
is below (A) on the precedence list.  The only exception is the 'OR'
operator.  This operator may be used in combination with any other
operator.  For example, '(ATOMIC OR NUCLEAR)(W)REACTOR' is valid.

=> s (antibod? or Fab) (10N) ((IL-12 (1N) p40))
L2           46 (ANTIBOD? OR FAB) (10N) ((IL-12 (1N) P40))

=> s (antibod? or Fab) (10N) ((IL (1N) B30))
L3            1 (ANTIBOD? OR FAB) (10N) ((IL (1N) B30))

=> s 13 not 12
L4            0 L3 NOT L2

=> dup rem 12
PROCESSING COMPLETED FOR L2
L5           15 DUP REM L2 (31 DUPLICATES REMOVED)

=> dis 13 ibib abs kwic

L3   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:        2001:185797  CAPLUS
DOCUMENT NUMBER:         134:236233
TITLE:                   Combinations of interleukin-12 p40 subunit with
                         interleukin B30, related reagents and therapeutic uses
                         thereof
INVENTOR(S):             Oppmann, Birgit; De Waal, Malefyt Rene; Rennick, Donna
                         M.; Kastelein, Robert A.; Wiekowski, Maria T.; Lira,
                         Sergio A.; Narula, Satwant K.
PATENT ASSIGNEE(S):      Schering Corp., USA
SOURCE:                  PCT Int. Appl., 69 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2001018051      A2   20010315       WO 2000-US24686  20000908
     WO 2001018051      A3   20010920
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL,
             IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK,
             MN, MX, MZ, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM,
             TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                    US 1999-393090    A  19990909
                                          US 1999-164616P   P  19991110
AB   Purified genes encoding cytokine from a mammal, reagents related thereto
     including purified proteins, specific antibodies, and nucleic acids
     encoding this mol. are provided.  The invention is specifically directed
     to compns. comprising combinations of IL-12 p40 subunit with interleukin
     B30 (IL-B30).  Observations indicate that the IL-12 p40/IL-B30 dimer is
     capable of inducing interferon-.gamma. prodn. by various cells.  Moreover,
     the IL-12 receptor .beta.1 subunit is a component od the receptor for the
     p40/IL-B30 dimer.  Methods of using said reagents and diagnostic kits are
     also provided.
IT   Immunoglobulins
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (Fv, Fab, or Fab2, IL-12 p40/IL-B30
        fusion protein binding compd. with; combinations of IL-12 p40 subunit
        with interleukin B30, related reagents and therapeutic uses thereof)
IT   Antibodies
     RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical
     study); BIOL (Biological study); USES (Uses)
        (IL-B30; combinations of IL-12 p40 subunit with
        interleukin B30, related reagents and therapeutic uses thereof)


=> dis 15 not 13
L3 IS NOT VALID HERE
For an explanation, enter "HELP DISPLAY".

=> s 15 not 13
L6           14 L5 NOT L3

=> dis 16 1-14 ibib abd kwic
'ABD' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid
in at least one of the files.  Refer to file specific help messages
or the STNGUIDE file for information on formats available in
individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):end

=> dis 16 1-14 ibib abs kwic

L6   ANSWER 1 OF 14      MEDLINE
ACCESSION NUMBER:    2002078602      IN-PROCESS
DOCUMENT NUMBER:     21663735    PubMed ID: 11805076
TITLE:               KM(+), a lectin from Artocarpus integrifolia, induces IL-12
                     p40 production by macrophages and switches from type 2 to
```

type 1 cell-mediated immunity against Leishmania major antigens, resulting in BALB/c mice resistance to infection.

AUTHOR: Panunto-Castelo A; Souza M A; Roque-Barreira M C; Silva J S
CORPORATE SOURCE: Departamento de Biologia Celular e Molecular e Bioagentes Patogenicos, Faculdade de Medicina de Ribeirao Preto, Universidade de Sao Paulo, Av. Bandeirantes 3900, Ribeirao Preto, SP 14040-900, Brazil.
SOURCE: GLYCOBIOLOGY, (2001 Dec) 11 (12) 1035-42.
Journal code: 9104124. ISSN: 0959-6658.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20020128
Last Updated on STN: 20020128

AB The outcome and severity of some diseases correlate with the dominance of either the T helper 1 (Th1) or Th2 immune response, which is stimulated by IL-12 or IL-4, respectively. In the present study we demonstrate that gamma interferon (IFN-gamma) secretion by murine spleen cells stimulated with KM(+), a mannose-binding lectin from Artocarpus integrifolia, is due to IL-12 induction, because (1) macrophages from several sources (including cell lines) produced IL-12 p40 in response to KM(+), and (2) lectin-free supernatants from J774 cell line cultures stimulated with KM(+) induced the secretion of IFN-gamma by spleen cell cultures, an effect blocked by the supernatant pretreatment with anti-IL-12 antibody. The known pattern of susceptibility of BALB/c mice to infection with Leishmania major, attributed to high levels of IL-4 production leading to a Th2 nonprotective immune response, was modified by administration of KM(+). Draining lymph node cells from these immunized BALB/c mice (in contrast to cells from animals immunized only with soluble leishmanial antigen [SLA]) secreted high levels of IFN-gamma and low levels of IL-4, which characterized a Th1 rather than a Th2 response pattern. The footpad thickness of BALB/c mice immunized with SLA plus KM(+) and challenged with L. major was similar to that of uninfected mice. This beneficial effect against leishmanial infection was blocked by pretreatment of these mice with anti-IL-12 **antibody**. These observations indicate that KM(+) induces **IL-12 p40** in vivo and has a protective effect against L. major infection.

AB . . . to that of uninfected mice. This beneficial effect against leishmanial infection was blocked by pretreatment of these mice with anti-IL-12 **antibody**. These observations indicate that KM(+) induces **IL-12 p40** in vivo and has a protective effect against L. major infection.

L6 ANSWER 2 OF 14 MEDLINE
ACCESSION NUMBER: 2001361390 MEDLINE
DOCUMENT NUMBER: 21317402 PubMed ID: 11422905
TITLE: Possible involvement of IL-12 in reovirus type-2-induced diabetes in newborn DBA/1 mice.
AUTHOR: Hayashi T; Morimoto M; Iwata H; Onodera T
CORPORATE SOURCE: Laboratory of Veterinary Pathology, Yamaguchi University, Yoshida, Yamaguchi 753-8515, Japan.. hayashi@agr.yamaguchi-u.ac.jp
SOURCE: SCANDINAVIAN JOURNAL OF IMMUNOLOGY, (2001 Jun) 53 (6) 572-8.
Journal code: UCW; 0323767. ISSN: 0300-9475.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010723
Last Updated on STN: 20010723
Entered Medline: 20010719

AB This study extends our previous observations that the reovirus type-2(Reo-2) can induce autoimmune insulitis, which may be mediated by T-helper (Th) 1-dependent mechanisms, resulting in diabetes in newborn DBA/1 mice. In this study mRNA expression for Th1-related cytokines including Th1 and Th2 cytokines in splenic cells was examined by reverse transcriptase polymerase chain reaction (RT-PCR) in relation to the development of insulitis. Furthermore, the effect of monoclonal **antibody** (MoAb) against interleukin (**IL**)-**12**(**p40**) on the development of insulitis and the mRNA expression in the splenic cells was examined. The mRNA expression for IL-12(p40), IL-18, and interferon (IFN)-gamma, but not IL-5, increased in the spleen in parallel with the development of insulitis. The treatment with MoAb to IL-12(p40) reduced the insulitis with diabetes which was associated with a decrease in the mRNA expression for IL-12(p40), IL-18 and IFN-gamma, and an increase of IL-4 mRNA expression in the spleen. The present study suggested that Th1-dominant systemic immune responses, being responsible for the development of autoimmune insulitis, might be induced by IL-12-induced and IL-18-activated mechanisms.

AB . . . examined by reverse transcriptase polymerase chain reaction (RT-PCR) in relation to the development of insulitis. Furthermore, the effect of monoclonal **antibody** (MoAb) against interleukin (**IL**)-**12**(**p40**) on the development of insulitis and the mRNA expression in the splenic cells was examined. The mRNA expression for IL-12(p40),. . .

L6 ANSWER 3 OF 14 MEDLINE
ACCESSION NUMBER: 2001292874 MEDLINE
DOCUMENT NUMBER: 21257998 PubMed ID: 11358987
TITLE: Interleukin-18 expression induced by Epstein-Barr virus-infected cells.
AUTHOR: Yao L; Setsuda J; Sgadari C; Cherney B; Tosato G
CORPORATE SOURCE: Transplantation Immunology Department, Medicine Branch, Division of Clinical Sciences, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA.. Yaol@mail.nih.gov
SOURCE: JOURNAL OF LEUKOCYTE BIOLOGY, (2001 May) 69 (5) 779-84.
Journal code: IWY; 8405628. ISSN: 0741-5400.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010709
Last Updated on STN: 20010830
Entered Medline: 20010705

AB Human Epstein-Barr virus (EBV)-negative Burkitt lymphomas cells usually grow as malignant subcutaneous tumors in athymic mice, but these tumors regress when the Burkitt cells are injected in conjunction with EBV-positive lymphoblastoid cells or when the Burkitt cells are

transfected with the EBV latent membrane protein-1 (LMP-1) gene. Tumor regression is mediated, in part, by murine interferon gamma (IFN-gamma) and the IFN-gamma-induced murine chemokine IFN-gamma-inducible protein-10 (IP-10). The mechanisms by which EBV-LMP-1 promotes the expression of IFN-gamma has remained unclear. Here we show that murine interleukin (IL)-18 was consistently expressed in regressing Burkitt tumors but was either expressed at low levels or absent from progressively growing Burkitt tumors. By immunohistochemical methods, IL-18 protein was visualized in regressing but not in progressively growing Burkitt tumors. In contrast, IL-12 p35 and IL-12 p40 were only rarely expressed in regressing Burkitt tumors. In splenocyte cultures, EBV-infected lymphoblastoid cells and LMP-1-transfected Burkitt cells promoted the expression of IL-18 but not the expression of IL-12 p35 and **IL-12 p40**. A neutralizing **antibody** directed at murine IL-18 reduced murine IP-10 expression induced by EBV-immortalized cells in splenocyte cultures. These results provide evidence for IL-18 expression in response to a viral latency protein and suggest that IL-18 may play an important role as an endogenous inducer of IFN-gamma expression, thereby contributing to tumor regression.

AB . . . EBV-infected lymphoblastoid cells and LMP-1-transfected Burkitt cells promoted the expression of IL-18 but not the expression of IL-12 p35 and **IL-12 p40**. A neutralizing **antibody** directed at murine IL-18 reduced murine IP-10 expression induced by EBV-immortalized cells in splenocyte cultures. These results provide evidence for. . .

L6 ANSWER 4 OF 14 MEDLINE

ACCESSION NUMBER:	2000042320 MEDLINE
DOCUMENT NUMBER:	20042320 PubMed ID: 10573524
TITLE:	Requirement for interleukin-12 in the pathogenesis of warm hepatic ischemia/reperfusion injury in mice.
AUTHOR:	Lentsch A B; Yoshidome H; Kato A; Warner R L; Cheadle W G; Ward P A; Edwards M J
CORPORATE SOURCE:	Department of Surgery, University of Louisville School of Medicine, Louisville, KY 40202, USA.. alentsch@louisville.edu
SOURCE:	HEPATOLOGY, (1999 Dec) 30 (6) 1448-53. Journal code: GBZ; 8302946. ISSN: 0270-9139.
PUB. COUNTRY:	United States Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	199912
ENTRY DATE:	Entered STN: 20000113 Last Updated on STN: 20000113 Entered Medline: 19991216

AB Hepatic ischemia and reperfusion causes neutrophil-dependent liver injury. Although the mechanisms of ischemia/reperfusion-induced liver neutrophil recruitment are somewhat understood, less is known regarding the early events that initiate the inflammatory injury. Using a murine model of partial hepatic ischemia and reperfusion, we evaluated the role of endogenous interleukin (IL)-12 in this inflammatory response. Hepatic ischemia for 90 minutes and reperfusion for up to 4 hours resulted in hepatocyte expression of IL-12. By 8 hours of reperfusion there were large increases in serum levels of interferon-gamma (IFNgamma) and tumor necrosis factor-alpha (TNFalpha). In addition, hepatic ischemia/reperfusion caused significant increases in liver neutrophil recruitment, hepatocellular injury, and liver edema, as defined by liver myeloperoxidase content, serum alanine aminotransferase, and liver wet to dry weight ratios, respectively. In mice treated with neutralizing **antibody** to IL-12 and in mice deficient in the **IL-12 p40** gene, ischemia/reperfusion-induced increases in IFNgamma and TNFalpha were greatly diminished. These conditions also caused significant reductions in liver myeloperoxidase content and attenuated the parameters of liver injury. The data suggest that IL-12 is required for the full induction of injury after hepatic ischemia and reperfusion.

AB . . . by liver myeloperoxidase content, serum alanine aminotransferase, and liver wet to dry weight ratios, respectively. In mice treated with neutralizing **antibody** to IL-12 and in mice deficient in the **IL-12 p40** gene, ischemia/reperfusion-induced increases in IFNgamma and TNFalpha were greatly diminished. These conditions also caused significant reductions in liver myeloperoxidase content. . .

L6 ANSWER 5 OF 14 MEDLINE

ACCESSION NUMBER:	1999441966 MEDLINE
DOCUMENT NUMBER:	99441966 PubMed ID: 10513808
TITLE:	Differential regulation of rheumatoid synovial cell interleukin-12 production by tumor necrosis factor alpha and CD40 signals.
AUTHOR:	Kitagawa M; Mitsui H; Nakamura H; Yoshino S; Miyakawa S; Ochiai N; Onobori M; Suzuki H; Sumida T
CORPORATE SOURCE:	Institute of Clinical Medicine, University of Tsukuba, Ibaraki, Japan.
SOURCE:	ARTHRITIS AND RHEUMATISM, (1999 Sep) 42 (9) 1917-26. Journal code: 90M; 0370605. ISSN: 0004-3591.
PUB. COUNTRY:	United States Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:	199910
ENTRY DATE:	Entered STN: 20000111 Last Updated on STN: 20000111 Entered Medline: 19991027

AB OBJECTIVE: To investigate the roles of tumor necrosis factor alpha(TNFalpha) and the CD40-CD154 interaction in interleukin-12 (IL-12) production by rheumatoid synovial cells (SC). METHODS: Levels of IL-12 (p40 and p70) in synovial tissue and culture supernatants of SC from patients with rheumatoid arthritis (RA), osteoarthritis (OA), and ankylosing spondylitis (AS) were assayed by enzyme-linked immunosorbent assay. Effects of anti-CD154 and anti-TNFalpha antibody on spontaneous and lipopolysaccharide (LPS)-stimulated IL-12 production by SC were examined. Effects of immobilized anti-CD3 treatment and depletion of CD4+ T cells on IL-12 production were also tested. CD154 expression by synovial T cells and intracellular IL-12 production during culture were analyzed by flow cytometry. RESULTS: IL-12 p40 and p70 levels in RA synovial tissue and spontaneous IL-12 p40 production by SC from RA patients were significantly higher than the levels in OA and AS patients. Spontaneous IL-12 production by SC from RA patients significantly decreased after depletion of CD4+ T cells from SC or after application of anti-CD154 antibody, but not by treatment with anti-TNFalpha **antibody**. Anti-CD3 **antibody** stimulation increased spontaneous **IL-12 p40**

production and CD154 expression by synovial T cells. The increment of **IL-12 p40** production by anti-CD3 was abrogated by anti-CD154 **antibody**. **IL-12 p40** production was also increased by LPS stimulation. LPS-stimulated IL-12 production was inhibited by anti-TNFalpha antibody, but not by T cell depletion and anti-CD154 **antibody** treatment. The TNFalpha inhibitor rolipram inhibited LPS-stimulated **IL-12 p40** production by RA SC more strongly than spontaneous production. TNFalpha restored LPS-stimulated IL-12 production that had been inhibited by rolipram. CONCLUSION: IL-12 production in RA is regulated by 2 different pathways. One pathway is T cell dependent, predominantly through a CD40-CD154 interaction, while the other is T cell independent, mediated through TNFalpha. Inhibition of IL-12 production by interference with CD40-CD154 interaction and TNFalpha production may be a potential therapeutic strategy for treating RA.

AB . . . after depletion of CD4+ T cells from SC or after application of anti-CD154 antibody, but not by treatment with anti-TNFalpha **antibody**. Anti-CD3 **antibody** stimulation increased spontaneous **IL-12 p40** production and CD154 expression by synovial T cells. The increment of **IL-12 p40** production by anti-CD3 was abrogated by anti-CD154 **antibody**. **IL-12 p40** production was also increased by LPS stimulation. LPS-stimulated IL-12 production was inhibited by anti-TNFalpha antibody, but not by T cell depletion and anti-CD154 **antibody** treatment. The TNFalpha inhibitor rolipram inhibited LPS-stimulated **IL-12 p40** production by RA SC more strongly than spontaneous production. TNFalpha restored LPS-stimulated IL-12 production that had been inhibited by rolipram.. . .

L6 ANSWER 6 OF 14 MEDLINE

ACCESSION NUMBER: 1999396467 MEDLINE
DOCUMENT NUMBER: 99396467 PubMed ID: 10455278
TITLE: IL-12 as a therapeutic target for pharmacological modulation in immune-mediated and inflammatory diseases: regulation of T helper 1/T helper 2 responses.
AUTHOR: Hasko G; Szabo C
CORPORATE SOURCE: Inotek Corp., 100 Cummings Center, Beverly, Massachusetts 01915, USA.. ghasko@inotekcorp.com
SOURCE: BRITISH JOURNAL OF PHARMACOLOGY, (1999 Jul) 127 (6) 1295-304. Ref: 129
Journal code: B00; 7502536. ISSN: 0007-1188.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 19991101
Last Updated on STN: 19991101
Entered Medline: 19991018

AB Interleukin-12 (IL-12) is a pivotal cytokine in driving the immune system towards a T helper (Th)1 type response and preventing a Th2 type immune profile. Therefore, IL-12 is indispensable in the defense against certain, mainly intracellular pathogens, but overproduction of this cytokine is crucially involved in the etiology of several inflammatory and autoimmune diseases. Hence, IL-12 is an ideal target for pharmacological intervention in the therapy of autoimmune and inflammatory diseases. The production of IL-12 and a resultant Th1 type immune response can be suppressed with several pharmacological approaches including modulation of intracellular cyclic AMP levels, glucocorticoids and nuclear factor-kappaB inhibition. IL-12 responsiveness may be inhibited using anti-IL-12 **antibodies**, soluble IL-12 receptors or the **IL-12 p40** homodimer. Exploitation of these approaches may provide novel means for the experimental therapy of a variety of pathophysiological states.

AB . . . approaches including modulation of intracellular cyclic AMP levels, glucocorticoids and nuclear factor-kappaB inhibition. IL-12 responsiveness may be inhibited using anti-IL-12 **antibodies**, soluble IL-12 receptors or the **IL-12 p40** homodimer. Exploitation of these approaches may provide novel means for the experimental therapy of a variety of pathophysiological states.

L6 ANSWER 7 OF 14 MEDLINE

ACCESSION NUMBER: 1999323829 MEDLINE
DOCUMENT NUMBER: 99323829 PubMed ID: 10394102
TITLE: Expression of B7-1, B7-2, and interleukin-12 in anti-Fas antibody-induced pulmonary fibrosis in mice.
AUTHOR: Kuwano K; Kaneko Y; Hagimoto N; Kawasaki M; Kunitake R; Tanaka T; Maeyama T; Miyazaki H; Matsuba T; Hara N
CORPORATE SOURCE: Research Institute for Diseases of the Chest, Faculty of Medicine, Kyushu University, Fukuoka, Japan.. kkuwano@kokyu.med.kyushu-u.ac.jp
SOURCE: INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (1999 Jun) 119 (2) 112-9.
Journal code: BJ7; 9211652. ISSN: 1018-2438.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990816
Last Updated on STN: 19990816
Entered Medline: 19990804

AB BACKGROUND: We have previously reported that the inhalation of anti-Fas antibody induced pulmonary fibrosis in mice. To induce an effective immune response, antigen-presenting cells have to not only present antigenic peptide with MHC molecules to T lymphocytes, but also express B7 costimulating molecules. The purpose of this study is to investigate whether B7 family costimulating molecules and interleukin-12 (IL-12), which primarily promote cellular immunity, are associated with anti-Fas antibody-induced pulmonary fibrosis. METHODS: We examined the expression of B7-1, B7-2, and IL-12 using the revese transcription-polymerase chain reaction (RT-PCR), RT-in situ PCR, and immunohistochemistry. RESULTS: We observed the upregulation of B7-1, B7-2, and **IL-12 p40** mRNA after anti-Fas **antibody** inhalation. B7-2 and **IL-12 p40** mRNA appeared to be expressed in mononuclear cells, while B7-1 mRNA and protein were expressed in bronchiolar epithelial cells as well as macrophages. CONCLUSION: These findings indicate that the T-cell-mediated immune response in this model involved the upregulation of B7-1, B7-2, and IL-12, and that the aberrant expression of B7-1 in bronchiolar epithelial cells may induce autoreactive T cell proliferation against themselves.

AB . . . the revese transcription-polymerase chain reaction (RT-PCR), RT-in situ PCR, and immunohistochemistry. RESULTS: We observed the upregulation of B7-1, B7-2, and **IL-12 p40** mRNA after anti-Fas **antibody** inhalation. B7-2 and **IL-12 p40** mRNA appeared to be expressed in mononuclear cells, while B7-1 mRNA and protein were expressed in bronchiolar epithelial cells as. . .

L6 ANSWER 8 OF 14 MEDLINE
ACCESSION NUMBER: 1999316963 MEDLINE
DOCUMENT NUMBER: 99316963 PubMed ID: 10390075
TITLE: Upregulation of antitumor immunity by IL-12 gene-transfected AK-5 tumor cells in vivo.
AUTHOR: Nandakumar K S; Lakshmi Rao K; Pardhasaradhi B V; Khar A
CORPORATE SOURCE: Centre for Cellular and Molecular Biology, Hyderabad, India.
SOURCE: CYTOKINES, CELLULAR AND MOLECULAR THERAPY, (1999 Mar) 5 (1) 7-14.
Journal code: CUS; 9713367. ISSN: 1368-4736.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 19991026
Last Updated on STN: 19991026
Entered Medline: 19991008

AB We have earlier demonstrated a significant role for IL-12 in the regression of a rat histiocytic tumor, AK-5. In order to analyze further the antitumor immunity induced by interleukin (IL)-12, we have established IL-12-secreting tumor cell clones by gene transfection. Significant enhancement in the lytic potential of splenocytes by the culture supernatants containing IL-12 demonstrated retention of biological activity by the tumor-cell-derived cytokine. Athymic nude mice transplanted subcutaneously with tumor cells engineered to secret IL-12 showed a significant reduction in tumor size, with enhanced antibody-dependent cellular cytotoxicity. Analysis of the serum samples from animals injected with the IL-12 gene-transfected AK-5 cells on different days revealed a significant increase in circulatory IL-12, interferon (IFN)-gamma, tumor necrosis factor (TNF)-alpha and antitumor antibodies, all of which contributed to the reduction in tumor mass. The enhanced proliferative capacity of splenocytes from these animals indicated the presence of highly activated immune cells in vivo. Similarly, intraperitoneal transplantation of IL-12 gene-transfected tumor cells in syngeneic Wistar rats induced a significant increase in cellular cytotoxicity, with a concomitant reduction in circulatory **IL-12 (p40)** protein. Administration of **antibodies** to IL-12 and IFN-gamma reduced the expression of the costimulatory molecules B7.1 and B7.2 and the cytolytic effectors granzyme B and Fas-L, suggesting their involvement in IFN-gamma-dependent antitumor immune response induced by IL-12. The present study thus demonstrates that IL-12 gene therapy could be among the promising approaches for an effective cancer therapy.

AB . . . gene-transfected tumor cells in syngeneic Wistar rats induced a significant increase in cellular cytotoxicity, with a concomitant reduction in circulatory **IL-12 (p40)** protein. Administration of **antibodies** to IL-12 and IFN-gamma reduced the expression of the costimulatory molecules B7.1 and B7.2 and the cytolytic effectors granzyme B. . .

L6 ANSWER 9 OF 14 MEDLINE
ACCESSION NUMBER: 1999120993 MEDLINE
DOCUMENT NUMBER: 99120993 PubMed ID: 9922218
TITLE: Interleukin-12 production by human alveolar macrophages is controlled by the autocrine production of interleukin-10.
AUTHOR: Isler P; de Rochemonteix B G; Songeon F; Boehringer N; Nicod L P
CORPORATE SOURCE: Pulmonary Division, University Hospital, Geneva, Switzerland.
SOURCE: AMERICAN JOURNAL OF RESPIRATORY CELL AND MOLECULAR BIOLOGY, (1999 Feb) 20 (2) 270-8.
Journal code: AOB; 8917225. ISSN: 1044-1549.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990324
Last Updated on STN: 19990324
Entered Medline: 19990311

AB By releasing interleukin (IL)-12 in the lung, alveolar macrophages (AM) may profoundly modify an immune response. The autocrine regulation of the heterodimeric, biologically active form of IL-12 (IL-12 p70) by IL-10 was studied, as well as the expression of its subunits of 35 kD (p35) and 40 kD (p40). AM cultured in medium alone expressed only p35 mRNA. Both p35 and p40 mRNA levels were induced by lipopolysaccharide (LPS) and were further increased by interferon-gamma (IFN-gamma). LPS alone induced IL-12 p40 but not IL-12 p70 production in monocytes and in AM. However, IL-12 p70 was released when the autocrine production of IL-10 was neutralized by IL-10 blocking **antibody**, and **IL-12 p40** production increased. Although IFN-gamma markedly decreased LPS-induced IL-10 production in AM, neutralizing IL-10 further enhanced the level of LPS and IFN-gamma-induced IL-12 p70 in AM. In contrast, neutralizing the trace amount of IL-10 released by AM stimulated by CD40 crosslinking and IFN-gamma did not increase IL-12 p70. Thus, IL-12 p70 production by AM appears to be tightly controlled by the autocrine release of IL-10 when stimulated by LPS, or by LPS and IFN-gamma, whereas CD40 crosslinking triggered IL-12 p70 production in the absence of autocrine regulation by IL-10.

AB . . . monocytes and in AM. However, IL-12 p70 was released when the autocrine production of IL-10 was neutralized by IL-10 blocking **antibody**, and **IL-12 p40** production increased. Although IFN-gamma markedly decreased LPS-induced IL-10 production in AM, neutralizing IL-10 further enhanced the level of LPS and. . .

L6 ANSWER 10 OF 14 MEDLINE
ACCESSION NUMBER: 97353200 MEDLINE
DOCUMENT NUMBER: 97353200 PubMed ID: 9209458
TITLE: Immunoregulation by B7 and IL-12 gene transfer.
AUTHOR: Kato K; Okumura K; Yagita H
CORPORATE SOURCE: Department of Immunology, Juntendo University School of Medicine, Tokyo, Japan.

SOURCE: LEUKEMIA, (1997 Apr) 11 Suppl 3 572-6.
Journal code: LEU; 8704895. ISSN: 0887-6924.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199708
ENTRY DATE: Entered STN: 19970813
Last Updated on STN: 19970813
Entered Medline: 19970807

AB Our recent studies using various costimulatory molecules have demonstrated that antitumor effect could be induced by B7- or B70-transduced mouse tumors. To augment antitumor effect in vivo, the combination therapy with a costimulatory gene and a cytokine, interkeukin 12 (IL-12), gene to treat metastatic mouse lung tumor was investigated. We transfected with mouse B7 and/or IL-12 into mouse lung carcinoma 3LL, and three transfectants (IL-12/3LL, B7/3LL and IL-12/B7/3LL) were generated. CTL activity induced by the inoculation of IL-12/B7/3LL was increased about 10-fold compared with parental 3LL inoculation. We then examined the therapeutic efficacy of combination with B7 and IL-12-transduced tumors. Four weeks after 3LL inoculation, lung metastasis was significantly reduced by IL-12/B7/3LL post-inoculation, indicating that potent therapeutic antitumor immunity can be induced by combination with costimulators B7 and IL-12. Recently, it was reported that p40 subunit of IL-12 appeared to be a specific inhibitor for IL-12 heterodimer in vitro. To clarify the biological functions of p40 in vivo, we generated the myoblast transfectants which produced IL-12 p40 alone. Local production of **IL-12 p40** from transfectant could suppress allogenic CTL induction and Th1-type **antibodies** (IgG2a/2b/3) production in vivo. Furthermore, **IL-12 p40** producing myoblast are less susceptible to rejection compared with parental myoblast, indicating that IL-12 p40 gene transfer may be useful therapeutically in Th1-mediated transplantation and autoimmune disorders.

AB . . . the biological functions of p40 in vivo, we generated the myoblast transfectants which produced IL-12 p40 alone. Local production of **IL-12 p40** from transfectant could suppress allogenic CTL induction and Th1-type **antibodies** (IgG2a/2b/3) production in vivo. Furthermore, **IL-12 p40** producing myoblast are less susceptible to rejection compared with parental myoblast, indicating that IL-12 p40 gene transfer may be useful. . .

L6 ANSWER 11 OF 14 MEDLINE
ACCESSION NUMBER: 96238996 MEDLINE
DOCUMENT NUMBER: 96238996 PubMed ID: 8675286
TITLE: Lipoteichoic acid preparations of gram-positive bacteria induce interleukin-12 through a CD14-dependent pathway.
AUTHOR: Cleveland M G; Gorham J D; Murphy T L; Tuomanen E; Murphy K M
CORPORATE SOURCE: Division of Dermatology, Department of Internal Medicine, Washington University School of Medicine, St. Louis, Missouri 63110, USA.
CONTRACT NUMBER: AI31238 (NIAID)
AI34580 (NIAID)
SOURCE: INFECTION AND IMMUNITY, (1996 Jun) 64 (6) 1906-12.
Journal code: GO7; 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199608
ENTRY DATE: Entered STN: 19960822
Last Updated on STN: 19960822
Entered Medline: 19960812

AB Interleukin 12 (IL-12) strongly augments gamma interferon production by natural killer (NK) and T cells. IL-12 also promotes effective cell-mediated immune responses, which are particularly important against intracellular bacteria such as Listeria monocytogenes. While the lipopolysaccharide (LPS) of gram-negative bacteria induces monocyte production of IL-12, the relevant gram-positive components which induce IL-12 production are uncharacterized. We used the human monocytic cell line THP-1 to study IL-12 induction by gram-positive bacteria. Muramyl dipeptides as well as the major muramyl tetrapeptide component of Streptococcus pneumoniae were inactive for inducing IL-12. In contrast, lipoteichoic acid (LTA), a predominant surface glycolipid of gram-positive bacteria, potently induced IL-12 p40 gene expression. A competitive LPS antagonist, Rhodobacter sphaeroides LPS, inhibited LTA-induced IL-12 production, suggesting a common pathway for LPS and LTA in IL-12 activation. Pretreatment of cells with anti-CD14 monoclonal **antibody** blocked both LPS and LTA induction of **IL-12 p40** expression. LTA also induced Th1 development in naive CD4 T cells by an IL-12-dependent mechanism, indicating direct induction of physiologic levels of IL-12. Together, these results show that LTA is a potent surface structure of gram-positive bacteria which induces IL-12 in monocytes through a CD14-mediated pathway.

AB . . . LTA-induced IL-12 production, suggesting a common pathway for LPS and LTA in IL-12 activation. Pretreatment of cells with anti-CD14 monoclonal **antibody** blocked both LPS and LTA induction of **IL-12 p40** expression. LTA also induced Th1 development in naive CD4 T cells by an IL-12-dependent mechanism, indicating direct induction of physiologic. . .

L6 ANSWER 12 OF 14 MEDLINE
ACCESSION NUMBER: 96189837 MEDLINE
DOCUMENT NUMBER: 96189837 PubMed ID: 8602990
TITLE: IL-12 is involved in the activation of CD3+ granular lymphocytes in patients with lymphoproliferative disease of granular lymphocytes.
AUTHOR: Zambello R; Trentin L; Cassatella M A; Raimondi R; Cerutti A; Enthammer C; Facco M; Agostini C; Semenzato G
CORPORATE SOURCE: Padua University School of Medicine, Department of Clinial Medicine, First Medical Clinic, Italy.
SOURCE: BRITISH JOURNAL OF HAEMATOLOGY, (1996 Feb) 92 (2) 308-14.
Journal code: AXC; 0372544. ISSN: 0007-1048.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199605
ENTRY DATE: Entered STN: 19960524
Last Updated on STN: 19960524
Entered Medline: 19960515

AB We investigated the effects of Il-12 on functional properties of CD3+ CD8+

granular lymphocytes (GL) of of patients with lymphoproliferative disease of granular lymphocytes (LDGL). To this aim, in 10 cases with clonal CD3+ GL proliferation (nine cases with an associated TCR alpha/beta receptor and one case with a TCR gamma/delta receptor) we studied the proliferative and cytotoxic activities of resting and alpha CD3 monoclonal antibody (mAb) activated cells in the presence of rIL-12 and anti-IL-12 blocking **antibodies**. Specific mRNA for **IL-12 p40** subunit was also investigated. Our results showed that rIL-12 increased the proliferation of alpha CD3 pre-stimulated GL (2 to 6 times). Further, anti-IL-12 antibodies partially inhibited alpha CD3-induced cell growth, suggesting a role for this cytokine in the alpha CD3-mediated GL activation. The addition of antibodies blocking the p55 and p75 chains of IL-2 receptor (IL-2R) did not inhibit the rIL-12-mediated cell proliferation, indicating that the activity of rIL-12 is dependent of IL-2 in the in vivo expanded GL of patients under study. Concerning the cytotoxic activity, rIL-12 increased the alpha CD3-mediated NK activity against K-562 target cells and alpha CD3 redirected cytotoxicity against P815 target cells. Molecular analysis pointed out that, following alpha CD3 stimulation, patients' GL increased the expression of specific mRNA for the p40 subunit of IL-12 as compared to baseline conditions. Our data indicate that IL-12 is involved in the mechanisms of activation of clonal CD3+ GL in patients with LDGL; these features are consistent with the possibility that this discrete subset of GL might represent in vivo primed cytotoxic T lymphocytes.

AB . . . cytotoxic activities of resting and alpha CD3 monoclonal antibody (mAb) activated cells in the presence of rIL-12 and anti-IL-12 blocking **antibodies**. Specific mRNA for **IL-12 p40** subunit was also investigated. Our results showed that rIL-12 increased the proliferation of alpha CD3 pre-stimulated GL (2 to 6. . .

L6 ANSWER 13 OF 14 MEDLINE

ACCESSION NUMBER: 95386964 MEDLINE
DOCUMENT NUMBER: 95386964 PubMed ID: 7658066
TITLE: Interleukin-12 treatment during immunization elicits a T helper cell type 1-like immune response in mice challenged with respiratory syncytial virus and improves vaccine immunogenicity.
AUTHOR: Tang Y W; Graham B S
CORPORATE SOURCE: Department of Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee 37232-2605, USA.
CONTRACT NUMBER: AI-33933 (NIAID)
AI-37216 (NIAID)
SOURCE: JOURNAL OF INFECTIOUS DISEASES, (1995 Sep) 172 (3) 734-8.
Journal code: IH3; 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199510
ENTRY DATE: Entered STN: 19951013
Last Updated on STN: 19951013
Entered Medline: 19951004

AB Adjuvant effects of exogenous interleukin (IL)-12 on induction of immune responses against respiratory syncytial virus (RSV) infection in mice were evaluated. Giving recombinant IL-12 at the time of immunization with a formalin-inactivated alum-precipitated RSV preparation resulted in significant reduction of virus replication in lungs 4 days after RSV challenge. Intraperitoneal or intramuscular IL-12 was effective when given at the time of immunization but not at the time of challenge. IL-12 treatment resulted in increased interferon-gamma mRNA in lungs, increased IgG2a RSV-specific **antibody** isotype utilization, and increased endogenous **IL-12 p40** mRNA expression. IL-12 treatment did not significantly affect clinical outcome or cytotoxic T lymphocyte activity. These data demonstrate that IL-12 has potent adjuvant effects that may be due to induction of T helper cell type 1-like immune responses.

AB . . . immunization but not at the time of challenge. IL-12 treatment resulted in increased interferon-gamma mRNA in lungs, increased IgG2a RSV-specific **antibody** isotype utilization, and increased endogenous **IL-12 p40** mRNA expression. IL-12 treatment did not significantly affect clinical outcome or cytotoxic T lymphocyte activity. These data demonstrate that IL-12. . .

L6 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:492730 CAPLUS
DOCUMENT NUMBER: 131:321282
TITLE: Roles of cytokines in host defense to bacterial infection in mice
AUTHOR(S): Nakane, Akio; Sasaki, Sanae; Miura, Tomisato; Mizuki, Mayuko; Yamada, Kyogo; Mizuki, Daisuke; Hasegawa, Suguru
CORPORATE SOURCE: Department of Bacteriology, Hirosaki University School of Medicine, Hirosaki, 036-8562, Japan
SOURCE: International Congress Series (1999), 1172(Molecular Medicine: Novel Findings of Gene Diagnosis, Regulation of Gene Expression, and Gene Therapy), 165-174
CODEN: EXMDA4; ISSN: 0531-5131
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Antigen-specific CD4+ helper T (Th) cell responses can be divided into Th1, and Th2, based on cytokine prodn. Differentiation of Th1 cells, which can produce IL-2, IFN-.gamma., and lymphotoxin, is driven by IL-12 and IFN-.gamma., while differentiation of Th2 cells, which produce IL-4, IL-5, IL-10, and IL-13, depends on IL-4. We studied the prodn. and roles of Th1- and Th2-derived cytokines in bacterial infections such as a facultative intracellular-growing Listeria monocytogenes (L. monocytogenes) and an extracellular-growing Staphylococcus aureus (S. aureus) in mice. Female C57BL/6, C57BL/6-IFN-.gamma.-/-, and ddY mice were used. Mice were infected i.v. (iv) with L. monocytogenes or S. aureus. Monoclonal **antibodies** (mAbs) against IFN-.gamma., IL-4, IL-10, and **IL-12 p40** were injected iv into mice 2 h before infection. Cytokines in the bloodstream, spleen exts., and spleen cell culture supernatants were estd. by ELISAs or RT-PCR. Th1-type responses were obsd. in vivo and in vitro in L. monocytogenes infected mice. IFN-.gamma.-/- mice were highly susceptible to L. monocytogenes infection, compared with IFN-.gamma.+/+ mice. Administration of anti-IFN-.gamma. mAb or anti-IL-12 mAb also attenuated antilisterial resistance and induced Th2-type responses in immunocompetent mice. On the other hand, Th2-type responses were obsd. in vitro in S. aureus infected mice. IFN-.gamma.-/- mice were more resistant to S. aureus infection, compared with IFN-.gamma.+/+ mice. Administration of anti-IL-4 mAb or anti-IL-10 mAb attenuated the host defense. These

results suggest that Th1-type cytokines are responsible for host defense to a facultative intracellular-growing L. monocytogenes. In contrast, host defense to an extracellular-growing S. aureus is shown to be dependent on Th2-type cytokines.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Antigen-specific CD4+ helper T (Th) cell responses can be divided into Th1, and Th2, based on cytokine prodn. Differentiation of Th1 cells, which can produce IL-2, IFN-.gamma., and lymphotoxin, is driven by IL-12 and IFN-.gamma., while differentiation of Th2 cells, which produce IL-4, IL-5, IL-10, and IL-13, depends on IL-4. We studied the prodn. and roles of Th1- and Th2-derived cytokines in bacterial infections such as a facultative intracellular-growing Listeria monocytogenes (L. monocytogenes) and an extracellular-growing Staphylococcus aureus (S. aureus) in mice. Female C57BL/6, C57BL/6-IFN-.gamma.-/-, and ddY mice were used. Mice were infected i.v. (iv) with L. monocytogenes or S. aureus. Monoclonal **antibodies** (mAbs) against IFN-.gamma., IL-4, IL-10, and **IL-12 p40** were injected iv into mice 2 h before infection. Cytokines in the bloodstream, spleen exts., and spleen cell culture supernatants were estd. by ELISAs or RT-PCR. Th1-type responses were obsd. in vivo and in vitro in L. monocytogenes infected mice. IFN-.gamma.-/- mice were highly susceptible to L. monocytogenes infection, compared with IFN-.gamma.+/+ mice. Administration of anti-IFN-.gamma. mAb or anti-IL-12 mAb also attenuated antilisterial resistance and induced Th2-type responses in immunocompetent mice. On the other hand, Th2-type responses were obsd. in vitro in S. aureus infected mice. IFN-.gamma.-/- mice were more resistant to S. aureus infection, compared with IFN-.gamma.+/+ mice. Administration of anti-IL-4 mAb or anti-IL-10 mAb attenuated the host defense. These results suggest that Th1-type cytokines are responsible for host defense to a facultative intracellular-growing L. monocytogenes. In contrast, host defense to an extracellular-growing S. aureus is shown to be dependent on Th2-type cytokines.

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     (FILE 'HOME' ENTERED AT 17:25:42 ON 13 MAY 2002)

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 17:26:00 ON 13 MAY 2002
L1           46 S (ANTIBOD? OR FAB) (10N) ((IL-12 (1N) P40) OR (IL (1N) B30))
L2           46 S (ANTIBOD? OR FAB) (10N) ((IL-12 (1N) P40))
L3            1 S (ANTIBOD? OR FAB) (10N) ((IL (1N) B30))
L4            0 S L3 NOT L2
L5           15 DUP REM L2 (31 DUPLICATES REMOVED)
L6           14 S L5 NOT L3

=> s oppmann B?/au or De Waal Malefyt R?/au or Rennick D?/au or Kastelein R?/au or Wickowski M?/au or Lira S?/au or Narula S?/au
L7         1800 OPPMANN B?/AU OR DE WAAL MALEFYT R?/AU OR RENNICK D?/AU OR KASTE
                LEIN R?/AU OR WICKOWSKI M?/AU OR LIRA S?/AU OR NARULA S?/AU

=> s l7 and ((IL (1N) 12) or (IB (1N) 30))
L8          111 L7 AND ((IL (1N) 12) OR (IB (1N) 30))

=> s l7 and ((IL (1N) 12 (1N) p40) or (IB (1N) 30) or
MISSING TERM AFTER 30) OR
Operators must be followed by a search term, L-number, or query name.

=> s l7 and ((IL (1N) 12 (1N) p40) or (IB (1N) 30)
UNMATCHED LEFT PARENTHESIS 'AND ((IL'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s l7 and ((IL (1N) 12 (1N) p40) or (IB (1N) 30))
L9            9 L7 AND ((IL (1N) 12 (1N) P40) OR (IB (1N) 30))

=>

=> dup rem l9
PROCESSING COMPLETED FOR L9
L10           4 DUP REM L9 (5 DUPLICATES REMOVED)

=> dis l10 1-4 ibib abs kwic
```

L10 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:185797 CAPLUS

DOCUMENT NUMBER: 134:236233

TITLE: Combinations of interleukin-12 p40 subunit with interleukin B30, related reagents and therapeutic uses thereof

INVENTOR(S): **Oppmann, Birgit; De Waal, Malefyt Rene; Rennick, Donna M.; Kastelein, Robert A.**; Wiekowski, Maria T.; **Lira, Sergio A.; Narula, Satwant K.**

PATENT ASSIGNEE(S): Schering Corp., USA

SOURCE: PCT Int. Appl., 69 pp. CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001018051	A2	20010315	WO 2000-US24686	20000908
WO 2001018051	A3	20010920		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-393090 A 19990909
US 1999-164616P P 19991110

AB Purified genes encoding cytokine from a mammal, reagents related thereto including purified proteins, specific antibodies, and nucleic acids encoding this mol. are provided. The invention is specifically directed to compns. comprising combinations of **IL-12 p40** subunit with interleukin B30 (IL-B30). Observations indicate that the **IL-12 p40**/IL-B30 dimer is capable of inducing interferon-.gamma. prodn. by various cells. Moreover,

the IL-12 receptor .beta.1 subunit is a component od the receptor for the p40/IL-B30 dimer. Methods of using said reagents and diagnostic kits are also provided.

IN **Oppmann, Birgit; De Waal, Malefyt Rene; Rennick, Donna M.; Kastelein, Robert A.;** Wiekowski, Maria T.; **Lira, Sergio A.; Narula, Satwant K.**

AB Purified genes encoding cytokine from a mammal, reagents related thereto including purified proteins, specific antibodies, and nucleic acids encoding this mol. are provided. The invention is specifically directed to compns. comprising combinations of **IL-12 p40** subunit with interleukin B30 (IL-B30). Observations indicate that the **IL-12 p40/IL**-B30 dimer is capable of inducing interferon-.gamma. prodn. by various cells. Moreover, the IL-12 receptor .beta.1 subunit is a component od the receptor for the p40/IL-B30 dimer. Methods of using said reagents and diagnostic kits are also provided.

IT Immunoglobulins
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(A, effect on; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Immunoglobulins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Fv, Fab, or Fab2, **IL-12 p40/IL**-B30 fusion protein binding compd. with; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Immunoglobulins
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(G, effect on; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Primate
(**IL-12 p40** and IL-B30 from; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Fusion proteins (chimeric proteins)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**IL-12 p40** with IL-B30; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Steroids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**IL-12 p40/IL**-B30 antagonist combined with; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Antiviral agents
Chemotherapy
Radiotherapy
(**IL-12 p40/IL**-B30 fusion protein combined with; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Interleukin 18
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**IL-12 p40/IL**-B30 fusion protein combined with; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Antibodies
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**IL-12 p40**; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Analgesics
Anti-inflammatory agents
(IL-B30 agonist in combination with; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Interleukins
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(IL-B30, and dimer with **IL-12 p40**; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Signal transduction, biological
(IL-B30, blocking of; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Antibodies
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(IL-B30; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Dermatitis
Inflammation
(acute, modulating; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Immunostimulants
(adjuvants, **IL-12 p40/IL**-B30 fusion protein combined with; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Autoimmune disease
(amelioration of; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Cytokines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(and agonist or antagonist, in combination with IL-B30 agonists; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Interleukin 10

Tumor necrosis factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antagonist of, **IL-12 p40/IL-B30** antagonist combined with; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Allergy
(antagonized allergic effect; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Neoplasm
(anti-tumor effect; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Virus
(anti-viral effect; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Drug delivery systems
(aq., carrier selected from water, saline, or buffer; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Bacteria (Eubacteria)
Prokaryote
(as expression host; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Eukaryote (Eukaryotae)
Insect (Insecta)
Yeast
(cell, as expression host; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Inflammation
(chronic, amelioration of; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Cell activation
Drug screening
Immunomodulators
Molecular cloning
Test kits
(combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(complex with antibody; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT cDNA sequences
(for **IL-12 p40** subunit and interleukin B30; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Gene, animal
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(for **IL-12 p40**; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Gene, animal
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(for IL-B30; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Digestive tract
(gastroenteritis, acute, modulating; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT T cell (lymphocyte)
(helper cell/inducer, TH1, enhance response; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Liver, disease
Lung, disease
(inflammation, acute, modulating; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Interleukin receptors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(interleukin 12, .beta. subunit, antibody against; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Animal cell
(mammalian, including human, as expression host; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Neutrophil
(maturation into platelets, accelerating; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Platelet (blood)
(maturation, accelerating; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT T cell (lymphocyte)
(memory, proliferation, induced by IL-B30 or its agonist; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Cell differentiation
(modulation; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Drug delivery systems
(nasal; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Protein sequences
(of **IL-12 p40** subunit and interleukin B30; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Drug delivery systems
(oral; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Interleukin 12
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(p40, and dimer with IL-B30; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Drug delivery systems
(parenterals; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Cell
(processes, physiol., modulation; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Drug delivery systems
(rectal; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Drug delivery systems
(topical; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Animal
(treating inflammation in; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Interferons
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(.gamma., increase in prodn. by cell, **IL-12 p40**/IL-B30 and; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT 220349-72-4P, Interleukin B30 (human precursor) 220349-75-7P, Interleukin B30 (mouse precursor)
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(amino acid sequence; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT 220349-68-8, DNA (human interleukin B30 cDNA) 220349-69-9
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(nucleotide sequence; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT 220349-68-8, DNA (human interleukin B30 cDNA) 220349-69-9
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(nucleotide sequence; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

L10 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:628071 CAPLUS
DOCUMENT NUMBER: 131:321311
TITLE: Induction of CD4+ T cell alloantigen-specific hyporesponsiveness by IL-10 and TGF-.beta.
AUTHOR(S): Zeller, Jay C.; Panoskaltsis-Mortari, Angela; Murphy, William J.; Ruscetti, Francis W.; **Narula, Satwant**; Roncarolo, Maria G.; Blazar, Bruce R.
CORPORATE SOURCE: Department of Pediatrics, Division of Bone Marrow Transplantation, University of Minnesota Cancer Center, Minneapolis, MN, 55455, USA
SOURCE: Journal of Immunology (1999), 163(7), 3684-3691
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Induction and maintenance of Ag-specific tolerance are pivotal for immune homeostasis, prevention of autoimmune disorders, and the goal of transplantation. Recent studies suggest that certain cytokines, notably IL-10 and TGF-.beta., may play a role in down-regulating immune functions. To further examine the role of cytokines in Ag-specific hyporesponsiveness, murine CD4+ T cells were exposed ex vivo to alloantigen-bearing stimulators in the presence of exogenous IL-10 and/or TGF-.beta.. Primary but not secondary alloantigen proliferative responses were inhibited by IL-10 alone. However, the combined addn. of IL-10 + TGF-.beta. markedly induced alloantigen hyporesponsiveness in both primary and secondary MLR cultures. Alloantigen-specific hyporesponsiveness was obsd. also under conditions in which nominal Ag responses were intact. In adoptive transfer expts., IL-10 + TGF-.beta.-treated CD4+ T cells, but not T cells treated with either cytokine alone, were markedly impaired in inducing graft-vs-host disease alloresponses to MHC class II disparate recipients. These data provide the first formal evidence that IL-10 and TGF-.beta. have at least an additive effect in inducing alloantigen-specific tolerance, and that in vitro cytokines can be exploited to suppress CD4+ T cell-mediated Ag-specific responses in vivo.
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
AU Zeller, Jay C.; Panoskaltsis-Mortari, Angela; Murphy, William J.; Ruscetti, Francis W.; **Narula, Satwant**; Roncarolo, Maria G.; Blazar, Bruce R.
IT Interleukin **12**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**p40**; IL-10 and TGF-.beta. in CD4+ T cell alloantigen-specific hyporesponsiveness and the expression of)

L10 ANSWER 3 OF 4 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1999003132 MEDLINE
DOCUMENT NUMBER: 99003132 PubMed ID: 9784526
TITLE: Resident enteric bacteria are necessary for development of spontaneous colitis and immune system activation in interleukin-10-deficient mice.
AUTHOR: Sellon R K; Tonkonogy S; Schultz M; Dieleman L A; Grenther W; Balish E; **Rennick D M**; Sartor R B
CORPORATE SOURCE: Department of Companion Animal and Special Species, Pathology and Parasitology, College of Veterinary Medicine,

North Carolina State University, Raleigh, North Carolina 27606, USA.

SOURCE: INFECTION AND IMMUNITY, (1998 Nov) 66 (11) 5224-31.
Journal code: G07; 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981123

AB Mice with targeted deletion of the gene for interleukin-10 (IL-10) spontaneously develop enterocolitis when maintained in conventional conditions but develop only colitis when kept in specific-pathogen-free (SPF) environments. This study tested the hypothesis that enteric bacteria are necessary for the development of spontaneous colitis and immune system activation in IL-10-deficient mice. IL-10-deficient mice were maintained in either SPF conditions or germfree conditions or were populated with bacteria known to cause colitis in other rodent models. IL-10-deficient mice kept in SPF conditions developed colitis in all segments of the colon (cecum and proximal and distal colon). These mice exhibited immune system activation as evidenced by increased expression of CD44 on CD4(+) T cells; increased mesenteric lymph node cell numbers; and increased production of immunoglobulin A (IgA), IgG1, and **IL-12 p40** from colon fragment cultures. Mice populated with bacterial strains, including Bacteroides vulgatus, known to induce colitis in other rodent models had minimal colitis. Germfree IL-10-deficient mice had no evidence of colitis or immune system activation. We conclude therefore that resident enteric bacteria are necessary for the development of spontaneous colitis and immune system activation in IL-10-deficient mice.

AU Sellon R K; Tonkonogy S; Schultz M; Dieleman L A; Grenther W; Balish E; **Rennick D M**; Sartor R B

AB . . . CD44 on CD4(+) T cells; increased mesenteric lymph node cell numbers; and increased production of immunoglobulin A (IgA), IgG1, and **IL-12 p40** from colon fragment cultures. Mice populated with bacterial strains, including Bacteroides vulgatus, known to induce colitis in other rodent models. . .

L10 ANSWER 4 OF 4 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 94065191 MEDLINE
DOCUMENT NUMBER: 94065191 PubMed ID: 7902377
TITLE: Effects of IL-13 on phenotype, cytokine production, and cytotoxic function of human monocytes. Comparison with IL-4 and modulation by IFN-gamma or IL-10.
AUTHOR: **de Waal Malefyt R**; Figdor C G; Huijbens R; Mohan-Peterson S; Bennett B; Culpepper J; Dang W; Zurawski G; de Vries J E
CORPORATE SOURCE: Department of Human Immunology, DNAX Research Institute of Molecular and Cellular Biology, Palo Alto, CA 94304-1104.
SOURCE: JOURNAL OF IMMUNOLOGY, (1993 Dec 1) 151 (11) 6370-81.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199401
ENTRY DATE: Entered STN: 19940201
Last Updated on STN: 19950206
Entered Medline: 19940106

AB Recently, we described the cloning and expression of a human cDNA which is the homologue to P600, a gene transcribed by mouse Th2 clones. Based on its activities on human monocytes and B cells this gene was designated IL-13. In the present study we investigated the effects of IL-13 alone or in combination with IL-4, IFN-gamma, or IL-10 on human monocytes. IL-13 induced significant changes in the phenotype of monocytes. Like IL-4, it enhanced the expression of CD11b, CD11c, CD18, CD29, CD49e (VLA-5), class II MHC, CD13, and CD23, whereas it decreased the expression of CD64, CD32, CD16, and CD14 in a dose-dependent manner. IL-13 induced up-regulation of class II MHC Ag and its down-regulatory effects on CD64, CD32, and CD16 expression were prevented by IL-10. IFN-gamma could also partially prevent the IL-13-induced down-regulation of CD64, but not that of CD32 and CD16. However, IL-13 strongly inhibited spontaneous and IL-10- or IFN-gamma-induced ADCC activity of human monocytes toward anti-D coated Rh+ erythrocytes, indicating that the cytotoxic activity of monocytes was inhibited. Furthermore, IL-13 inhibited production of IL-1 alpha, IL-1 beta, IL-6, IL-8, IL-10, IL-**12** p35, **IL-12 p40**, macrophage inflammatory protein-1 alpha, granulocyte/macrophage-CSF, granulocyte-CSF, IFN-alpha, and TNF alpha by monocytes activated with LPS. In contrast, IL-13 enhanced the production of IL-1 ra by these cells. Similar results on cytokine production were observed or have been obtained with IL-4. Thus IL-13 shares most of its activities on human monocytes with IL-4, but no additive or synergistic effects of IL-4 and IL-13 on human monocytes were observed, suggesting that these cytokines may share common receptor components. Taken together, these results indicate that IL-13 has anti-inflammatory and important immunoregulatory activities.

AU **de Waal Malefyt R**; Figdor C G; Huijbens R; Mohan-Peterson S; Bennett B; Culpepper J; Dang W; Zurawski G; de Vries. . .

AB . . . that the cytotoxic activity of monocytes was inhibited. Furthermore, IL-13 inhibited production of IL-1 alpha, IL-1 beta, IL-6, IL-8, IL-10, IL-**12** p35, **IL-12 p40**, macrophage inflammatory protein-1 alpha, granulocyte/macrophage-CSF, granulocyte-CSF, IFN-alpha, and TNF alpha by monocytes activated with LPS. In contrast, IL-13 enhanced the. . .

```
=> dis his

     (FILE 'HOME' ENTERED AT 17:25:42 ON 13 MAY 2002)

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 17:26:00 ON 13 MAY 2002
L1            46 S (ANTIBOD? OR FAB) (10N) ((IL-12 (1N) P40) OR (IL (1N) B30))
L2            46 S (ANTIBOD? OR FAB) (10N) ((IL-12 (1N) P40))
L3             1 S (ANTIBOD? OR FAB) (10N) ((IL (1N) B30))
L4             0 S L3 NOT L2
L5            15 DUP REM L2 (31 DUPLICATES REMOVED)
L6            14 S L5 NOT L3
L7          1800 S OPPMANN B?/AU OR DE WAAL MALEFYT R?/AU OR RENNICK D?/AU OR KA
L8           111 S L7 AND ((IL (1N) 12) OR (IB (1N) 30))
L9             9 S L7 AND ((IL (1N) 12 (1N) P40) OR (IB (1N) 30))
L10            4 DUP REM L9 (5 DUPLICATES REMOVED)
```

```
=> s l7 and ((IL (1N) 12 (1N) p40) or (IL (1N) B30))
L11          11 L7 AND ((IL (1N) 12 (1N) P40) OR (IL (1N) B30))

=> dup rem l11
PROCESSING COMPLETED FOR L11
L12           6 DUP REM L11 (5 DUPLICATES REMOVED)

=> dis l12 1-6 ibib abs kwic
```

L12 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2002 ACS

```
ACCESSION NUMBER:        2001:185797  CAPLUS
DOCUMENT NUMBER:         134:236233
TITLE:                   Combinations of interleukin-12 p40 subunit with
                         interleukin B30, related reagents and therapeutic uses
                         thereof
INVENTOR(S):             Oppmann, Birgit; De Waal, Malefyt
                         Rene; Rennick, Donna M.;
                         Kastelein, Robert A.; Wiekowski, Maria T.;
                         Lira, Sergio A.; Narula, Satwant K.
PATENT ASSIGNEE(S):      Schering Corp., USA
SOURCE:                  PCT Int. Appl., 69 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.       KIND  DATE           APPLICATION NO.  DATE
     ---------------  ----  --------       ---------------  --------
     WO 2001018051     A2   20010315       WO 2000-US24686  20000908
     WO 2001018051     A3   20010920
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL,
             IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK,
             MN, MX, MZ, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM,
             TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                    US 1999-393090    A  19990909
                                          US 1999-164616P   P  19991110
```

AB Purified genes encoding cytokine from a mammal, reagents related thereto including purified proteins, specific antibodies, and nucleic acids encoding this mol. are provided. The invention is specifically directed to compns. comprising combinations of **IL-12 p40** subunit with interleukin **B30** (**IL-B30**). Observations indicate that the **IL-12 p40/IL-B30** dimer is capable of inducing interferon-.gamma. prodn. by various cells. Moreover, the IL-12 receptor .beta.1 subunit is a component od the receptor for the p40/**IL-B30** dimer. Methods of using said reagents and diagnostic kits are also provided.

IN **Oppmann, Birgit; De Waal, Malefyt Rene; Rennick, Donna M.; Kastelein, Robert A.**; Wiekowski, Maria T.; **Lira, Sergio A.; Narula, Satwant K.**

AB Purified genes encoding cytokine from a mammal, reagents related thereto including purified proteins, specific antibodies, and nucleic acids encoding this mol. are provided. The invention is specifically directed to compns. comprising combinations of **IL-12 p40** subunit with interleukin **B30** (**IL-B30**). Observations indicate that the **IL-12 p40/IL-B30** dimer is capable of inducing interferon-.gamma. prodn. by various cells. Moreover, the IL-12 receptor .beta.1 subunit is a component od the receptor for the p40/**IL-B30** dimer. Methods of using said reagents and diagnostic kits are also provided.

IT Immunoglobulins
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(A, effect on; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Immunoglobulins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Fv, Fab, or Fab2, **IL-12 p40/IL-B30** fusion protein binding compd. with; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Immunoglobulins
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(G, effect on; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Primate
(**IL-12 p40** and **IL-B30** from; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Fusion proteins (chimeric proteins)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**IL-12 p40** with **IL-B30** ; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Steroids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**IL-12 p40/IL-B30** antagonist combined with; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Antiviral agents
Chemotherapy
Radiotherapy
(**IL-12 p40/IL-B30** fusion protein combined with; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Interleukin 18
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**IL-12 p40/IL-B30** fusion protein combined with; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and

therapeutic uses thereof)
IT Antibodies
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**IL-12 p40**; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Analgesics
Anti-inflammatory agents
(**IL-B30** agonist in combination with; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Interleukins
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(**IL-B30**, and dimer with **IL-12 p40**; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Signal transduction, biological
(**IL-B30**, blocking of; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Antibodies
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**IL-B30**; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Dermatitis
Inflammation
(acute, modulating; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Immunostimulants
(adjuvants, **IL-12 p40/IL-B30** fusion protein combined with; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Autoimmune disease
(amelioration of; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Cytokines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(and agonist or antagonist, in combination with **IL-B30** agonists; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Interleukin 10
Tumor necrosis factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antagonist of, **IL-12 p40/IL-B30** antagonist combined with; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Allergy
(antagonized allergic effect; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Neoplasm
(anti-tumor effect; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Virus
(anti-viral effect; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Drug delivery systems
(aq., carrier selected from water, saline, or buffer; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Bacteria (Eubacteria)
Prokaryote
(as expression host; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Eukaryote (Eukaryotae)
Insect (Insecta)
Yeast
(cell, as expression host; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Inflammation
(chronic, amelioration of; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Cell activation
Drug screening
Immunomodulators
Molecular cloning
Test kits
(combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(complex with antibody; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT cDNA sequences
(for **IL-12 p40** subunit and interleukin B30; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Gene, animal
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(for **IL-12 p40**; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)
IT Gene, animal
RL BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological

study); USES (Uses)
(for **IL-B30**; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Digestive tract
(gastroenteritis, acute, modulating; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT T cell (lymphocyte)
(helper cell/inducer, TH1, enhance response; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Liver, disease
Lung, disease
(inflammation, acute, modulating; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Interleukin receptors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(interleukin 12, .beta. subunit, antibody against; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Animal cell
(mammalian, including human, as expression host; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Neutrophil
(maturation into platelets, accelerating; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Platelet (blood)
(maturation, accelerating; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT T cell (lymphocyte)
(memory, proliferation, induced by **IL-B30** or its agonist; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Cell differentiation
(modulation; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Drug delivery systems
(nasal; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Protein sequences
(of **IL-12 p40** subunit and interleukin B30; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Drug delivery systems
(oral; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Interleukin 12
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(p40, and dimer with **IL-B30**; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Drug delivery systems
(parenterals; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Cell
(processes, physiol., modulation; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Drug delivery systems
(rectal; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Drug delivery systems
(topical; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Animal
(treating inflammation in; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT Interferons
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(.gamma., increase in prodn. by cell, **IL-12 p40/IL-B30** and; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT 220349-72-4P, Interleukin B30 (human precursor) 220349-75-7P, Interleukin B30 (mouse precursor)
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(amino acid sequence; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT 220349-68-8, DNA (human interleukin B30 cDNA) 220349-69-9
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(nucleotide sequence; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

IT 220349-68-8, DNA (human interleukin B30 cDNA) 220349-69-9
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(nucleotide sequence; combinations of **IL-12 p40** subunit with interleukin B30, related reagents and therapeutic uses thereof)

L12 ANSWER 2 OF 6 CAPLUS
ACCESSION NUMBER: 1999:511252 CAPLUS
DOCUMENT NUMBER: 131:143528

TITLE: Mammalian cytokine receptor proteins and their cDNA sequences and interleukin-B30 ligands
INVENTOR(S): Mattson, Jeanine D.; McClanahan, Terrill K.; **Kastelein, Robert A.**
PATENT ASSIGNEE(S): Schering Corp., USA
SOURCE: PCT Int. Appl., 133 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9940195	A1	19990812	WO 1999-US2600	19990205
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9926611	A1	19990823	AU 1999-26611	19990205

PRIORITY APPLN. INFO.:

US 1998-73941P	P	19980206
US 1998-78194	A	19980513
WO 1999-US2600	W	19990205

AB Nucleic acids encoding mammalian, e.g., human or mouse, cytokine receptor proteins designated DNAX Cytokine Receptor Subunit 1 (DCRS1) or DNAX Sol. Receptor Subunit 1 (DSRS1) which bind to the cytokine interleukin-B30 (**IL-B30**). DSRS1 aligns with and exhibits features in common with other cytokine receptor .alpha.-type subunits and is believed to interact with the corresponding DCRS1 to forma a functional receptor when the receptor ligand is present. DCRS1 shows relatively close similarity with gp130, which is the .beta.-subunit of the interleukin-6 receptor. The ligand for the receptor is likely that designated **IL-B30**, whose sequence is near that of G-CSF and interleukin-6. Antibodies, both polyclonal and monoclonal, are also provided. Methods of using the compns. for both diagnostic and therapeutic utilities are provided.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IN Mattson, Jeanine D.; McClanahan, Terrill K.; **Kastelein, Robert A.**

AB Nucleic acids encoding mammalian, e.g., human or mouse, cytokine receptor proteins designated DNAX Cytokine Receptor Subunit 1 (DCRS1) or DNAX Sol. Receptor Subunit 1 (DSRS1) which bind to the cytokine interleukin-B30 (**IL-B30**). DSRS1 aligns with and exhibits features in common with other cytokine receptor .alpha.-type subunits and is believed to interact with the corresponding DCRS1 to forma a functional receptor when the receptor ligand is present. DCRS1 shows relatively close similarity with gp130, which is the .beta.-subunit of the interleukin-6 receptor. The ligand for the receptor is likely that designated **IL-B30**, whose sequence is near that of G-CSF and interleukin-6. Antibodies, both polyclonal and monoclonal, are also provided. Methods of using the compns. for both diagnostic and therapeutic utilities are provided.

L12 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:628071 CAPLUS
DOCUMENT NUMBER: 131:321311
TITLE: Induction of CD4+ T cell alloantigen-specific hyporesponsiveness by IL-10 and TGF-.beta.
AUTHOR(S): Zeller, Jay C.; Panoskaltsis-Mortari, Angela; Murphy, William J.; Ruscetti, Francis W.; **Narula, Satwant**; Roncarolo, Maria G.; Blazar, Bruce R.
CORPORATE SOURCE: Department of Pediatrics, Division of Bone Marrow Transplantation, University of Minnesota Cancer Center, Minneapolis, MN, 55455, USA
SOURCE: Journal of Immunology (1999), 163(7), 3684-3691
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Induction and maintenance of Ag-specific tolerance are pivotal for immune homeostasis, prevention of autoimmune disorders, and the goal of transplantation. Recent studies suggest that certain cytokines, notably IL-10 and TGF-.beta., may play a role in down-regulating immune functions. To further examine the role of cytokines in Ag-specific hyporesponsiveness, murine CD4+ T cells were exposed ex vivo to alloantigen-bearing stimulators in the presence of exogenous IL-10 and/or TGF-.beta.. Primary but not secondary alloantigen proliferative responses were inhibited by IL-10 alone. However, the combined addn. of IL-10 + TGF-.beta. markedly induced alloantigen hyporesponsiveness in both primary and secondary MLR cultures. Alloantigen-specific hyporesponsiveness was obsd. also under conditions in which nominal Ag responses were intact. In adoptive transfer expts., IL-10 + TGF-.beta.-treated CD4+ T cells, but not T cells treated with either cytokine alone, were markedly impaired in inducing graft-vs-host disease alloresponses to MHC class II disparate recipients. These data provide the first formal evidence that IL-10 and TGF-.beta. have at least an additive effect in inducing alloantigen-specific tolerance, and that in vitro cytokines can be exploited to suppress CD4+ T cell-mediated Ag-specific responses in vivo.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AU Zeller, Jay C.; Panoskaltsis-Mortari, Angela; Murphy, William J.; Ruscetti, Francis W.; **Narula, Satwant**; Roncarolo, Maria G.; Blazar, Bruce R.

IT Interleukin **12**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**p40**; **IL**-10 and TGF-.beta. in CD4+ T cell alloantigen-specific hyporesponsiveness and the expression of)

L12 ANSWER 4 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:467482 BIOSIS
DOCUMENT NUMBER: PREV200000467482
TITLE: Expression of the novel cytokine **IL-B30** in transgenic mice induces a multi-organ inflammatory disease.
AUTHOR(S): Wiekowski, M. (1); Leach, M.; Evans, E.; Sullivan, L. (1); Chen, S. (1); Yang, T. (1); **Kastelein, R.**; **Narula, S. (1)**; **Lira, S. A. (1)**
CORPORATE SOURCE: (1) Dpt of Immunology, Schering-Plough Research Institute,

2015 Galloping Hill Rd., Kenilworth, NJ, 07033 USA

SOURCE: Cytokine, (Nov., 1999) Vol. 11, No. 11, pp. 968. print. Meeting Info.: Seventh Annual Conference of the International Cytokine Society Hilton Head, South Carolina, USA December 5-9, 1999 The International Cytokine Society . ISSN: 1043-4666.

DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

TI Expression of the novel cytokine **IL-B30** in transgenic mice induces a multi-organ inflammatory disease.

AU Wiekowski, M. (1); Leach, M.; Evans, E.; Sullivan, L. (1); Chen, S. (1); Yang, T. (1); **Kastelein, R.; Narula, S. (1)**; **Lira, S. A. (1)**

L12 ANSWER 5 OF 6 MEDLINE DUPLICATE 1

ACCESSION NUMBER: 1999003132 MEDLINE
DOCUMENT NUMBER: 99003132 PubMed ID: 9784526
TITLE: Resident enteric bacteria are necessary for development of spontaneous colitis and immune system activation in interleukin-10-deficient mice.
AUTHOR: Sellon R K; Tonkonogy S; Schultz M; Dieleman L A; Grenther W; Balish E; **Rennick D M**; Sartor R B
CORPORATE SOURCE: Department of Companion Animal and Special Species, Pathology and Parasitology, College of Veterinary Medicine, North Carolina State University, Raleigh, North Carolina 27606, USA.
SOURCE: INFECTION AND IMMUNITY, (1998 Nov) 66 (11) 5224-31. Journal code: G07; 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981123

AB Mice with targeted deletion of the gene for interleukin-10 (IL-10) spontaneously develop enterocolitis when maintained in conventional conditions but develop only colitis when kept in specific-pathogen-free (SPF) environments. This study tested the hypothesis that enteric bacteria are necessary for the development of spontaneous colitis and immune system activation in IL-10-deficient mice. IL-10-deficient mice were maintained in either SPF conditions or germfree conditions or were populated with bacteria known to cause colitis in other rodent models. IL-10-deficient mice kept in SPF conditions developed colitis in all segments of the colon (cecum and proximal and distal colon). These mice exhibited immune system activation as evidenced by increased expression of CD44 on CD4(+) T cells; increased mesenteric lymph node cell numbers; and increased production of immunoglobulin A (IgA), IgG1, and **IL-12 p40** from colon fragment cultures. Mice populated with bacterial strains, including Bacteroides vulgatus, known to induce colitis in other rodent models had minimal colitis. Germfree IL-10-deficient mice had no evidence of colitis or immune system activation. We conclude therefore that resident enteric bacteria are necessary for the development of spontaneous colitis and immune system activation in IL-10-deficient mice.

AU Sellon R K; Tonkonogy S; Schultz M; Dieleman L A; Grenther W; Balish E; **Rennick D M**; Sartor R B

AB . . . CD44 on CD4(+) T cells; increased mesenteric lymph node cell numbers; and increased production of immunoglobulin A (IgA), IgG1, and **IL-12 p40** from colon fragment cultures. Mice populated with bacterial strains, including Bacteroides vulgatus, known to induce colitis in other rodent models. . .

L12 ANSWER 6 OF 6 MEDLINE DUPLICATE 2

ACCESSION NUMBER: 94065191 MEDLINE
DOCUMENT NUMBER: 94065191 PubMed ID: 7902377
TITLE: Effects of IL-13 on phenotype, cytokine production, and cytotoxic function of human monocytes. Comparison with IL-4 and modulation by IFN-gamma or IL-10.
AUTHOR: **de Waal Malefyt R**; Figdor C G; Huijbens R; Mohan-Peterson S; Bennett B; Culpepper J; Dang W; Zurawski G; de Vries J E
CORPORATE SOURCE: Department of Human Immunology, DNAX Research Institute of Molecular and Cellular Biology, Palo Alto, CA 94304-1104.
SOURCE: JOURNAL OF IMMUNOLOGY, (1993 Dec 1) 151 (11) 6370-81. Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199401
ENTRY DATE: Entered STN: 19940201
Last Updated on STN: 19950206
Entered Medline: 19940106

AB Recently, we described the cloning and expression of a human cDNA which is the homologue to P600, a gene transcribed by mouse Th2 clones. Based on its activities on human monocytes and B cells this gene was designated IL-13. In the present study we investigated the effects of IL-13 alone or in combination with IL-4, IFN-gamma, or IL-10 on human monocytes. IL-13 induced significant changes in the phenotype of monocytes. Like IL-4, it enhanced the expression of CD11b, CD11c, CD18, CD29, CD49e (VLA-5), class II MHC, CD13, and CD23, whereas it decreased the expression of CD64, CD32, CD16, and CD14 in a dose-dependent manner. IL-13 induced up-regulation of class II MHC Ag and its down-regulatory effects on CD64, CD32, and CD16 expression were prevented by IL-10. IFN-gamma could also partially prevent the IL-13-induced down-regulation of CD64, but not that of CD32 and CD16. However, IL-13 strongly inhibited spontaneous and IL-10- or IFN-gamma-induced ADCC activity of human monocytes toward anti-D coated Rh+ erythrocytes, indicating that the cytotoxic activity of monocytes was inhibited. Furthermore, IL-13 inhibited production of IL-1 alpha, IL-1 beta, IL-6, IL-8, IL-10, IL-12 p35, **IL-12 p40**, macrophage inflammatory protein-1 alpha, granulocyte/macrophage-CSF, granulocyte-CSF, IFN-alpha, and TNF alpha by monocytes activated with LPS. In contrast, IL-13 enhanced the production of IL-1 ra by these cells. Similar results on cytokine production were observed or have been obtained with IL-4. Thus IL-13 shares most of its activities on human monocytes with IL-4, but no additive or synergistic effects of IL-4 and IL-13 on human monocytes were observed, suggesting that these cytokines may share common receptor components. Taken together, these results indicate that IL-13 has anti-inflammatory and important immunoregulatory activities.

AU **de Waal Malefyt R**, Figdor C G; Huijbens R; Mohan-Peterson S;

```
     Bennett B; Culpepper J; Dang W; Zurawski G; de Vries. . . .
AB   . . . that the cytotoxic activity of monocytes was inhibited.
     Furthermore, IL-13 inhibited production of IL-1 alpha, IL-1 beta, IL-6,
     IL-8, IL-10, IL-12 p35, IL-12 p40,
     macrophage inflammatory protein-1 alpha, granulocyte/macrophage-CSF,
     granulocyte-CSF, IFN-alpha, and TNF alpha by monocytes activated with LPS.
     In contrast, IL-13 enhanced the. . .


=> dis his

     (FILE 'HOME' ENTERED AT 17:25:42 ON 13 MAY 2002)

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 17:26:00 ON 13 MAY 2002
L1            46 S (ANTIBOD? OR FAB) (10N) ((IL-12 (1N) P40) OR (IL (1N) B30))
L2            46 S (ANTIBOD? OR FAB) (10N) ((IL-12 (1N) P40))
L3             1 S (ANTIBOD? OR FAB) (10N) ((IL (1N) B30))
L4             0 S L3 NOT L2
L5            15 DUP REM L2 (31 DUPLICATES REMOVED)
L6            14 S L5 NOT L3
L7          1800 S OPPMANN B?/AU OR DE WAAL MALEFYT R?/AU OR RENNICK D?/AU OR KA
L8           111 S L7 AND ((IL (1N) 12) OR (IB (1N) 30))
L9             9 S L7 AND ((IL (1N) 12 (1N) P40) OR (IB (1N) 30))
L10            4 DUP REM L9 (5 DUPLICATES REMOVED)
L11           11 S L7 AND ((IL (1N) 12 (1N) P40) OR (IL (1N) B30))
L12            6 DUP REM L11 (5 DUPLICATES REMOVED)

=> end
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y
COST IN U.S. DOLLARS                                 SINCE FILE      TOTAL
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